

AMENDMENTS

IN THE CLAIMS

33. (Currently Amended) A method of screening a substance substances for an ability to affect TRRE TNF receptor releasing activity, comprising:

- a) incubating TNF receptor or cells expressing TNF receptor with the substance and with a polypeptide an isolated polypeptide that causes TNF receptor to be cleaved in the absence of the substance;
- b) measuring any TNF receptor cleaved; and
- c) correlating any increase or decrease of the receptor cleaved by the peptide polypeptide with an ability of the substance to enhance or diminish TRRE TNF receptor releasing activity ; wherein the polypeptide has at least one of the following properties:
 - i) it comprises an amino acid sequence selected from SEQ. ID NOs: 151, 153, and 154;
 - ii) it comprises a fragment of any one of SEQ. ID NOs: 151, 153, or 154 that causes increased release of TNF receptor from human cells in which TNF receptor is expressed;
 - iii) it comprises an amino acid sequence encoded in any one of SEQ. ID NOs:1, 5, 6, 8, 9, or 10; or
 - iv) it comprises an amino acid sequence that causes increased release of TNF receptor from human cells in which TNF receptor is expressed, and is encoded by a polynucleotide that hybridizes-at 30°C in 6 × SSC containing 50% formamide to a polynucleotide having a sequence selected from SEQ. ID NOs:1, 5, 6, 8, 9, or 10.

34. (Withdrawn) The screening method of claim 33, wherein the polypeptide contains SEQ. ID NOs: 147-149, 151, or 153-154, or fragment thereof which causes increased release of TNF receptor from human cells in which TNF receptor is expressed.

35. **(Currently Amended)** The screening method of claim 33, wherein the polypeptide has at least one of the following properties:

- i) it comprises a sequence encoded in the longest open reading frame of SEQ. ID NOs: **1-10 or a fragment thereof 1, 5, 6, 8, 9, or 10 or fragment of any of these sequences; or**
- ii) it is encoded by a polynucleotide that hybridizes at 30°C in 6 × SSC containing 50% formamide to a polynucleotide having a sequence selected from SEQ. ID NOs: **1-10 1, 5, 6, 8, 9, or 10;**
and wherein the polypeptide causes increased release of TNF receptor from human cells in which TNF receptor is expressed.

36. *(Previously Presented)* The screening method of claim 33, wherein the polypeptide has been obtained by purifying TRRE from human cells that express it endogenously.

37. *(Previously Presented)* The screening method of claim 33, wherein the polypeptide has been obtained by expressing a recombinant polynucleotide.

38. *(Previously Presented)* The screening method of claim 33, wherein the polypeptide has metalloprotease activity.

39. **(Currently Amended)** The screening method of claim 35, wherein the polynucleotide comprises a sequence selected from the longest open reading frame of SEQ. ID NOs: **1-10 or fragment thereof 1, 5, 6, 8, 9, or 10, or a fragment of any of these sequences.**

40. **(Currently Amended)** The screening method of claim 35, wherein the polynucleotide hybridizes **under stringent conditions at 30°C in 6 × SSC containing 50% formamide** to a polynucleotide having a sequence selected from SEQ. ID NOs: **1-10 1, 5, 6, 8, 9, or 10, or a fragment of any of these sequences.**

41. *(Withdrawn)* The screening method of claim 35, wherein the polynucleotide comprises the sequence of the longest open reading frame of SEQ. ID NO:1 or fragment thereof.

42. *(Withdrawn)* The screening method of claim 35, wherein the polynucleotide comprises the sequence of the longest open reading frame of SEQ. ID NO:5 or fragment thereof.
43. *(Withdrawn)* The screening method of claim 35, wherein the polynucleotide comprises the sequence of the longest open reading frame of SEQ. ID NO:6 or fragment thereof.
44. *(Withdrawn)* The screening method of claim 35, wherein the polynucleotide comprises the sequence of the longest open reading frame of SEQ. ID NO:8 or fragment thereof.
45. *(Previously Presented)* The screening method of claim 35, wherein the polynucleotide comprises the sequence of the longest open reading frame of SEQ. ID NO:9 or fragment thereof.
46. *(Withdrawn)* The screening method of claim 35, wherein the polynucleotide comprises the sequence of the longest open reading frame of SEQ. ID NO:10 or fragment thereof.
47. ***(Withdrawn) (Currently Amended)*** The screening method of claim 35 33, wherein the polynucleotide hybridizes under stringent conditions at 30°C in 6 × SSC containing 50% formamide to a polynucleotide having the sequence of SEQ. ID NO:1.
48. ***(Withdrawn) (Currently Amended)*** The screening method of claim 35 33, wherein the polynucleotide hybridizes under stringent conditions at 30°C in 6 × SSC containing 50% formamide to a polynucleotide having the sequence of SEQ. ID NO:5.
49. ***(Withdrawn) (Currently Amended)*** The screening method of claim 35 33, wherein the polynucleotide hybridizes under stringent conditions at 30°C in 6 × SSC containing 50% formamide to a polynucleotide having the sequence of SEQ. ID NO:6.
50. ***(Withdrawn) (Currently Amended)*** The screening method of claim 35 33, wherein the polynucleotide hybridizes under stringent conditions at 30°C in 6 × SSC containing 50% formamide to a polynucleotide having the sequence of SEQ. ID NO:8.

51. **(Currently Amended)** The screening method of claim 35 33, wherein the polynucleotide hybridizes ~~under stringent conditions at 30°C in 6 × SSC containing 50% formamide~~ to a polynucleotide having the sequence of SEQ. ID NO:9.
52. **(Withdrawn) (Currently Amended)** The screening method of claim 35 33, wherein the polynucleotide hybridizes ~~under stringent conditions at 30°C in 6 × SSC containing 50% formamide~~ to a polynucleotide having the sequence of SEQ. ID NO:10.
53. *(Previously Presented)* The screening method of claim 33, wherein the substance is incubated with p55 TNF receptor in step a).
54. *(Previously Presented)* The screening method of claim 33, wherein the substance is incubated with p75 TNF receptor in step a).
55. *(Previously Presented)* The screening method of claim 33, wherein the substance is incubated with a cell expressing p55 TNF receptor in step a).
56. *(Previously Presented)* The screening method of claim 33, wherein the substance is incubated with a cell expressing p75 TNF receptor in step a).
57. *(Previously Presented)* The screening method of claim 33, wherein the measuring of TNF receptor cleaved in step b) comprises measuring binding capacity for TNF on the surface of the treated cell.
58. *(Previously Presented)* The screening method of claim 33, wherein the measuring of TNF receptor cleaved in step b) comprises measuring the concentration of soluble TNF receptor in culture medium from the treated cell.
59. *(New)* The screening method of claim 33, wherein the polypeptide comprises SEQ. ID NO:151 or fragment thereof.

60. *(New)* The screening method of claim 33, wherein the polypeptide comprises SEQ. ID NO:153 or fragment thereof.
61. *(New)* The screening method of claim 33, wherein the polypeptide comprises SEQ. ID NO:154 or fragment thereof.